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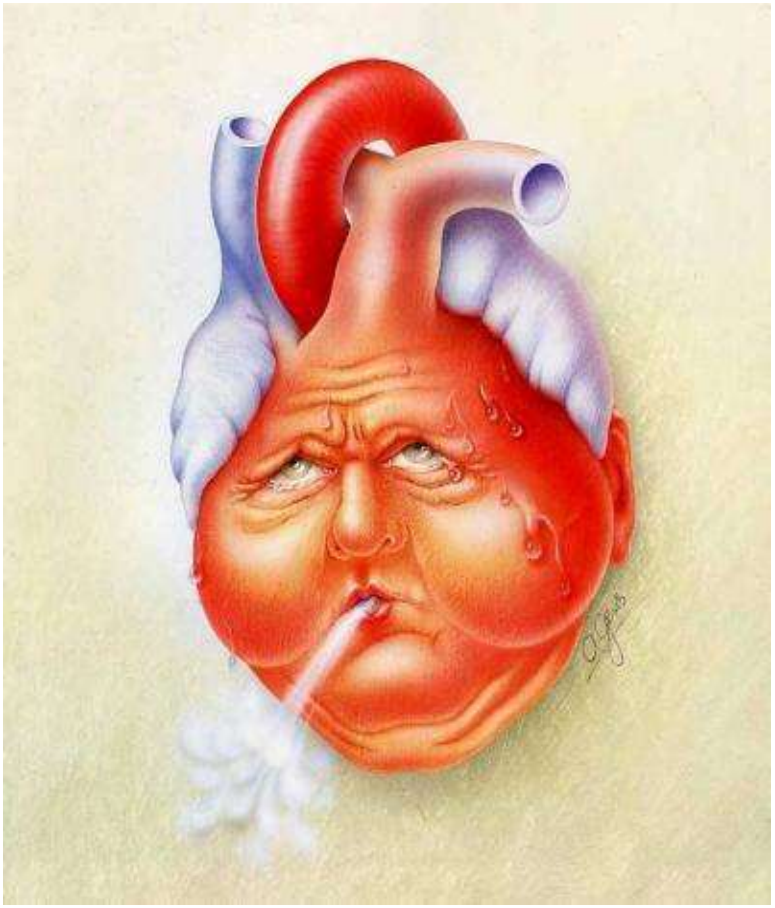
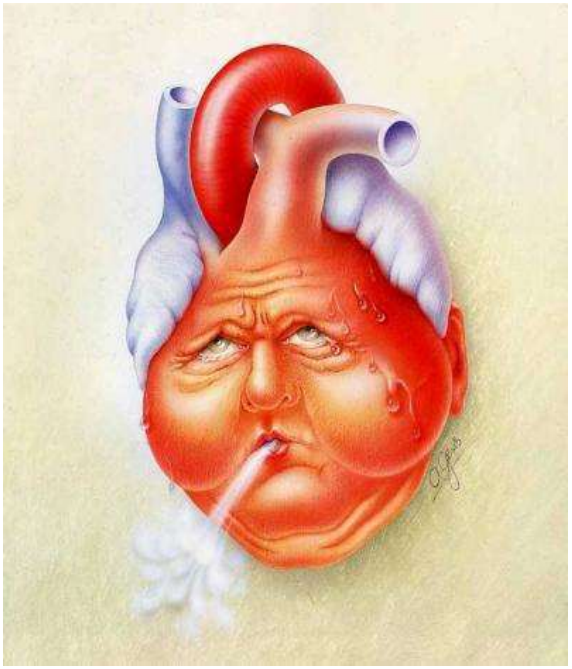
Part 6: Chronic Heart Failure Continued



Karen Kopacek, M.S., R.Ph.
Associate Professor (CHS)
Spring 2021

HF Part 6



- Medication therapies for stages in the development and progression of HF
  - Stage C meds: ARNI, hydralazine-isosorbide, and AA (or MRA)
- Patient case continued

HF Case: Part 2

- SB is a 64 yo female who presents to clinic complaining of SOB with getting dressed and difficulty sleeping at night due to coughing.
- She notices her ankles are swollen and her socks leave a pronounced mark on her legs.
- She feels nauseous and gets full after eating only half of her meals.
- She can't exercise lately due to fatigue and weakness.

HF Case Continued

- Physical exam
  - Vitals: BP 108/72 mmHg, HR 92 bpm, RR 16 breaths/min
  - Ht: 66 inches, wt 71 kg ("dry" weight 68kg)
  - HEENT: JVP 10cm water
  - Heart: RRR, S3 present
  - Abd: soft, nontender, normal bowel sounds
  - Ext: 2+ pitting edema bilaterally
  - Lungs: Clear
- Chest X-ray: cardiomegaly
- ECHO: EF 20%

HF Case Continued

Home medications include:

- Atorvastatin 40mg po qhs
- ~~Diltiazem SR 240mg po bid~~
- Isosorbide mononitrate 120mg po qam
- Nitroglycerin 0.4mg SL PRN CP
- Lansoprazole 30mg po qhs
- Aspirin 81mg po qday
- ~~Ibuprofen 400mg po PRN headaches~~

Question #4

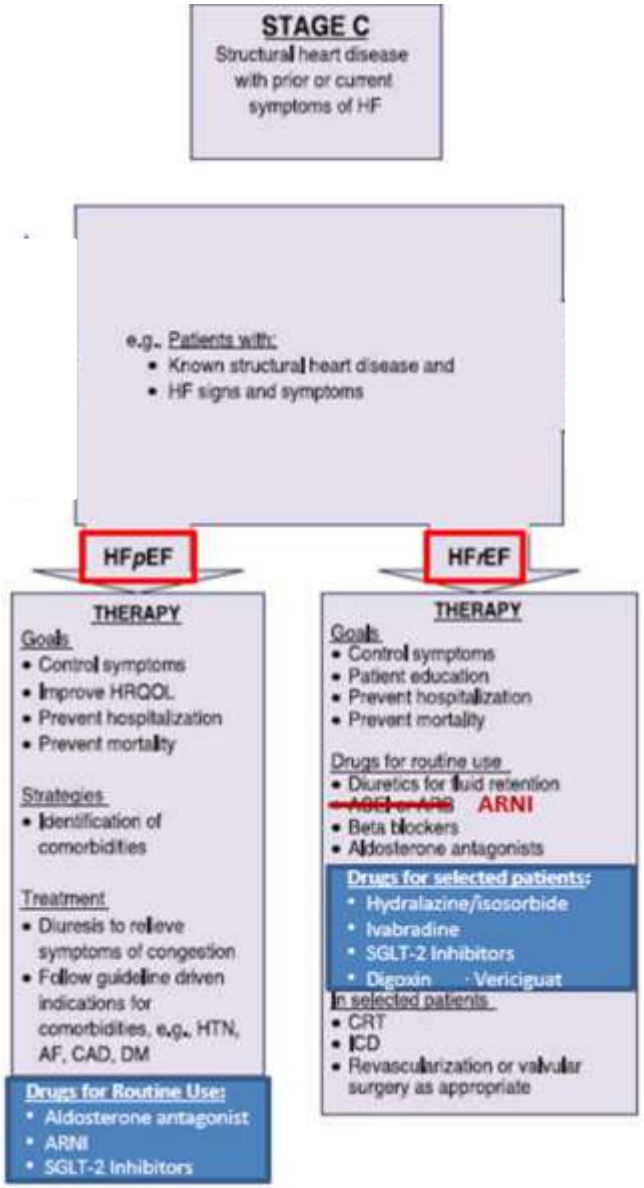
- Which of the following medications is most appropriate for treating SB's congestion?
  a. Hydrochlorothiazide 25 mg daily
  b. Furosemide 20mg BID
  c. Spironolactone 25 mg daily
  d. Metolazone 5 mg daily
  e. Eplerenone 50 mg daily

Question #5

- She is currently not receiving any guideline directed medications for HF. What medication(s) should you consider starting once she is at or near euvolemic?
  a. Carvedilol
  b. Lisinopril
  c. Metoprolol tartrate
  d. Valsartan

Stage C – Has/Had HF Symptoms

- Diuretics
- SGLT-2 inhibitors
- **ARNI**
- **Hydralazine/isosorbide**
- **Aldosterone Antagonists**
- Ivabradine
- Digoxin
- Vericiguat
- Device therapy



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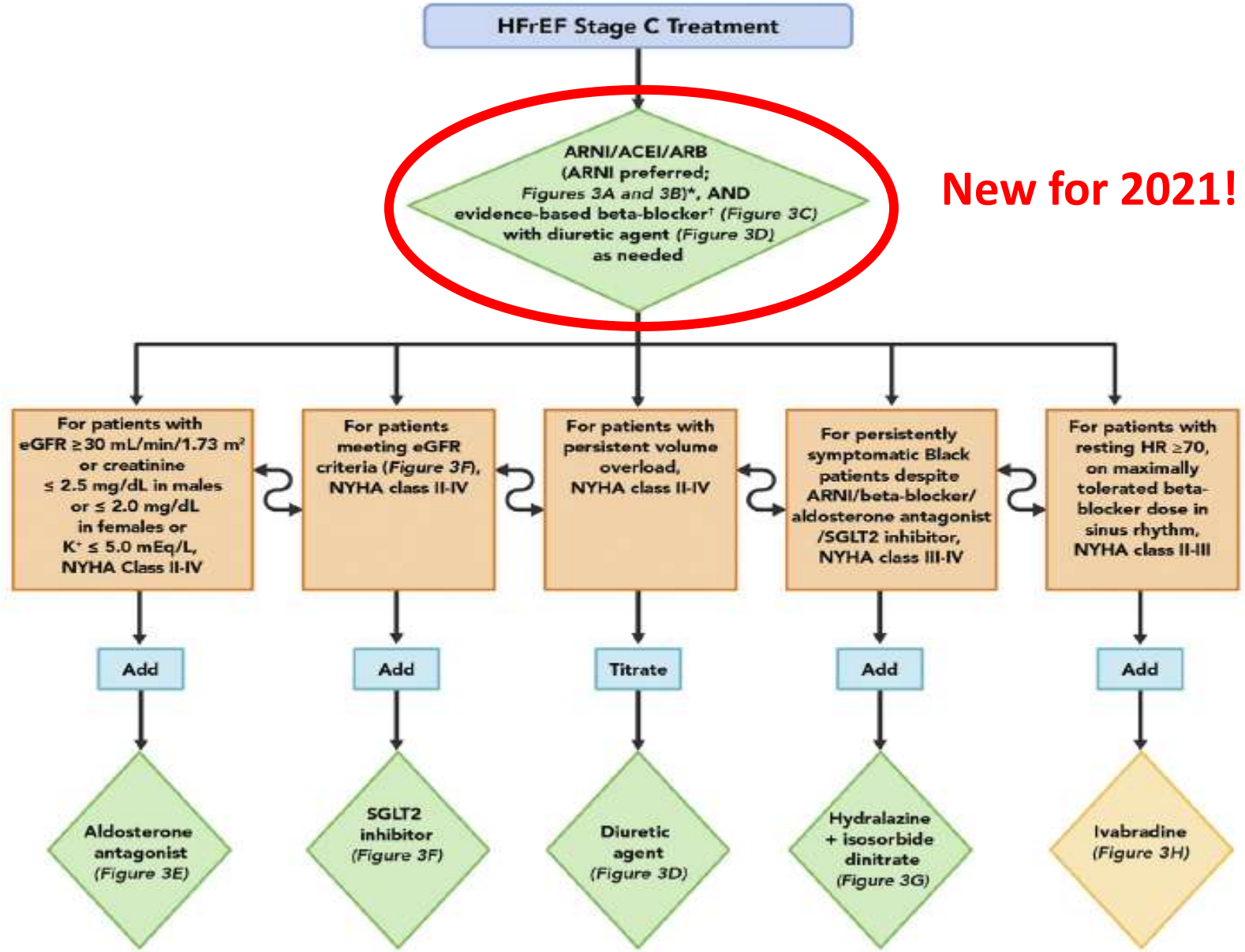

New for 2021!

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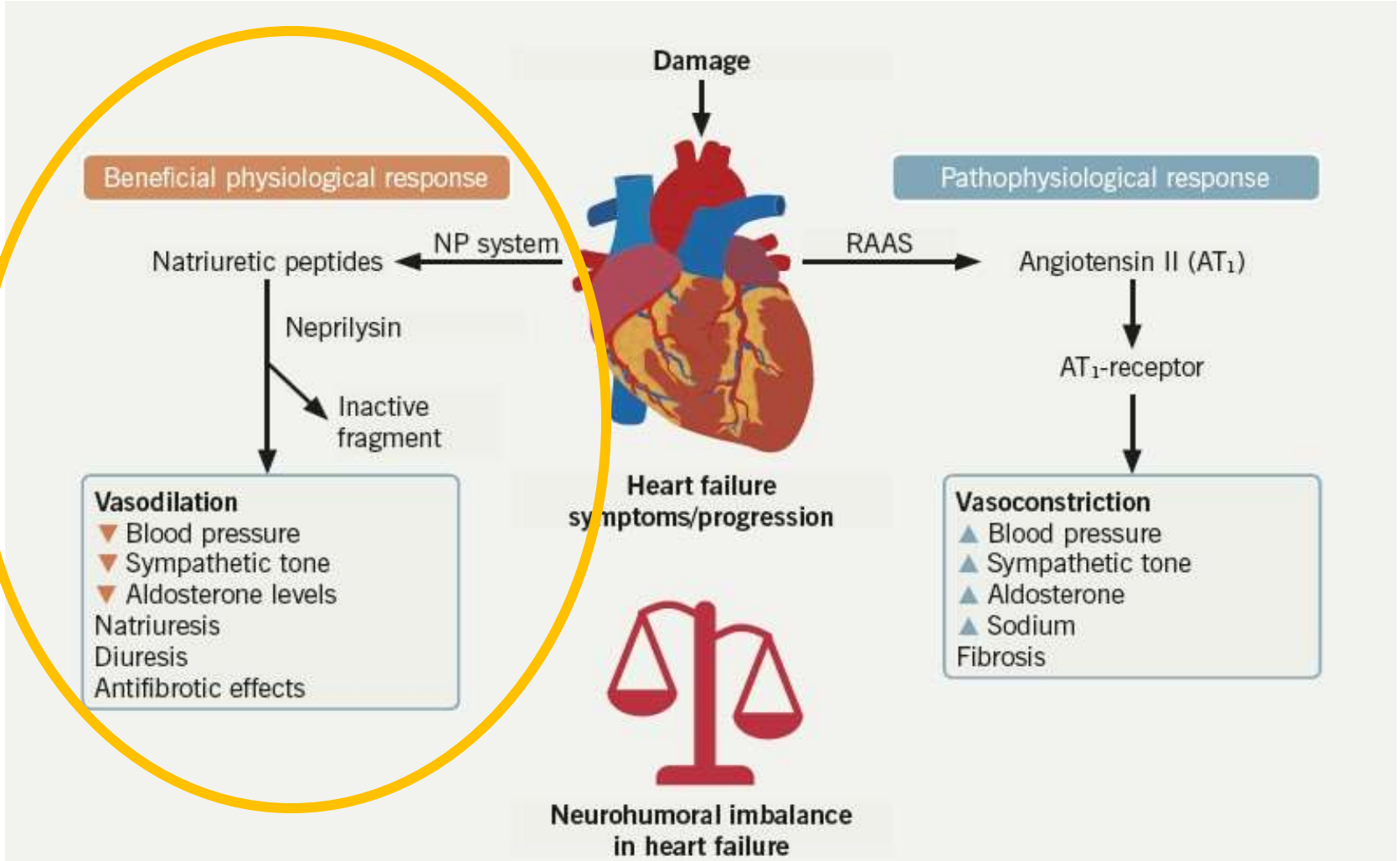
2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment

Valsartan/Sacubitril (Entresto®)

- Indication: Stage C HF*r*EF NYHA class II-III used in place of ACEI/ARB along with other GDMT
- MOA: sacubitril inhibits the enzyme neprilysin to increase levels of natriuretic peptides (NP)
  - NP are a group of hormones whose stimulation and release is due to high filling pressures and stretching of atrial and ventricular cardiomyocytes
  - NP work to counter effect of ATII to improve vasodilation, natriuresis, and diuresis

Neurohumoral Imbalance in HF



Adapted from Langenickel TH, Dole WP. Angiotensin receptor-neprilysin inhibition with LCZ696: a novel approach for the treatment of heart failure. *Drug Discovery Today: Therapeutic Strategies* 2012;9:e131–e139.

Key: NP = natriuretic peptide; RAAS = renin-angiotensin-aldosterone-system

Valsartan/Sacubitril (Entresto®)

- Dosing: depends if patient already taking an ACEI or ARB:
  - Must allow 36-hour washout period before switching from ACEI to ARNI due to angioedema (NO WASHOUT FOR ARB)
  - Double the dose every 2 weeks to target dose

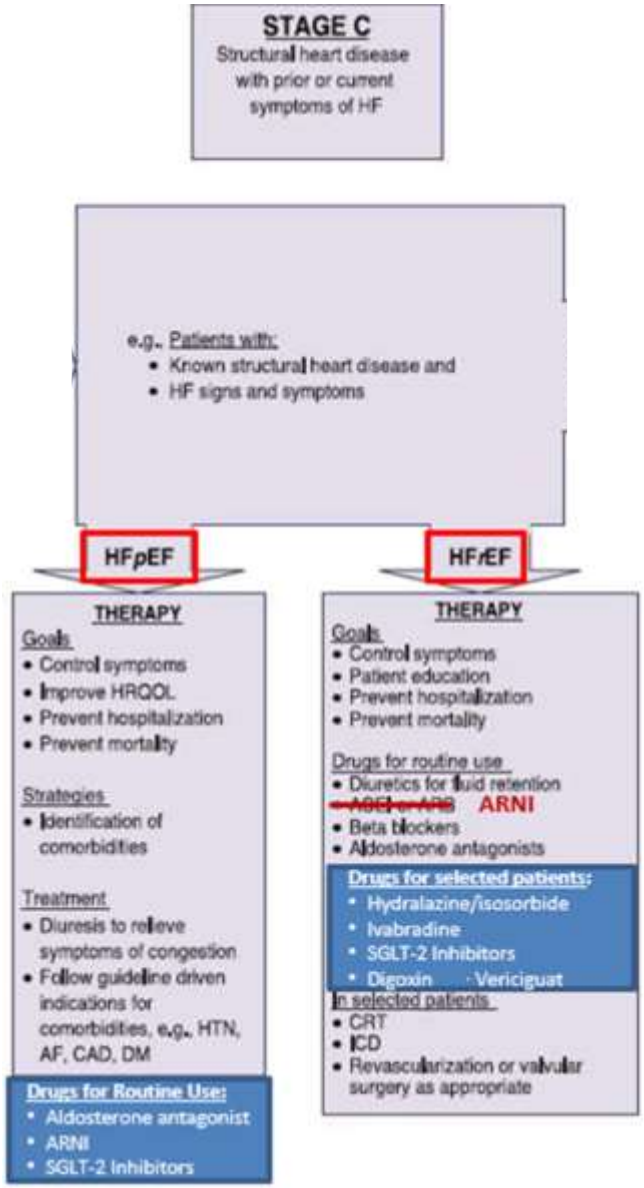
	Initial Dose	Target Dose
ACEI/ARB naïve, taking equivalent ≤ 10mg enalapril daily or ≤ valsartan 160mg/day, elderly (≥ 75 yrs), or CrCL < 30 ml/min	Sacubitril 24mg/ valsartan 26mg BID	**Sacubitril 97mg/ valsartan 103mg BID**
Switching from ACEI/ARB (taking Equivalent to > 10mg enalapril or > 160mg valsartan/day)	Sacubitril 49mg/ valsartan 51mg BID	

Valsartan/Sacubitril (Entresto®)

- Cannot monitor BNP levels as it increases during Entresto therapy, must use NT-proBNP
- Side effects: hypotension (both drugs lower BP!)
  - May need to lower diuretic dose (avoid hypovolemia), adjust doses of other drugs that lower BP, or decrease Entresto dose
- Same SE as ACEI/ARB monotherapy:
  - Hyperkalemia, kidney function decline
  - Higher risk for angioedema than ARB alone; do not use in patients with history of angioedema
- Similar drug interactions as ACEI/ARB

Stage C – Has/Had HF Symptoms

- Diuretics
- SGLT-2 inhibitors
- ARNI
- **Hydralazine/isosorbide**
- Aldosterone Antagonists
- Ivabradine
- Digoxin
- Vericiguat
- Device therapy



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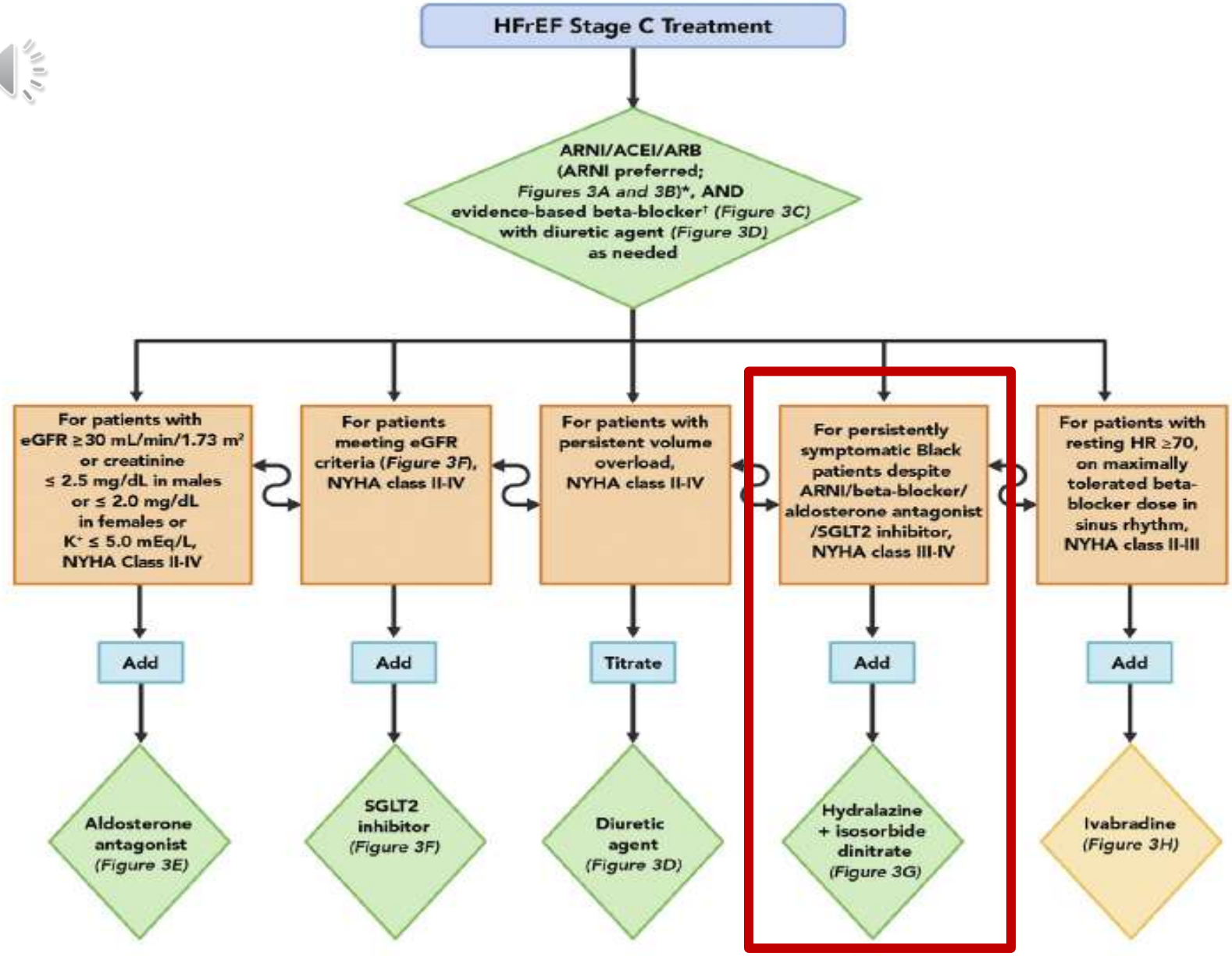

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2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment

Hydralazine/ISDN

- Two indications for use:
  1. Patients intolerant to ACEI/ARB (V-HeFT I and II trials)
  2. May add to GDMT therapies in Black patients with Stage C HFrEF who remain symptomatic (NYHA Class III-IV

- Mechanism of action in HF:
  - Hydralazine is a direct vasodilator (↓ afterload)
  - ISDN increases NO concentration (↓ preload and afterload)
  - Combination reduces resistance to left ventricular ejection, increases stroke volume, and decreases ventricular filling pressure

Hydralazine/ISDN Dosing in HF*r*EF

	Initial Dose	Target Dose
Hydralazine/ISDN combo tablet	37.5mg/20mg TID	75mg/40mg TID
Hydralazine and ISDN or ISMN	25mg TID 20mg TID or 30mg QD	75mg TID 40mg TID or 120mg QD

2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment

Stage C – Has/Had HF Symptoms

- Diuretics
- SGLT-2 inhibitors
- ARNI
- Hydralazine/isosorbide
- **Aldosterone Antagonists**
- Ivabradine
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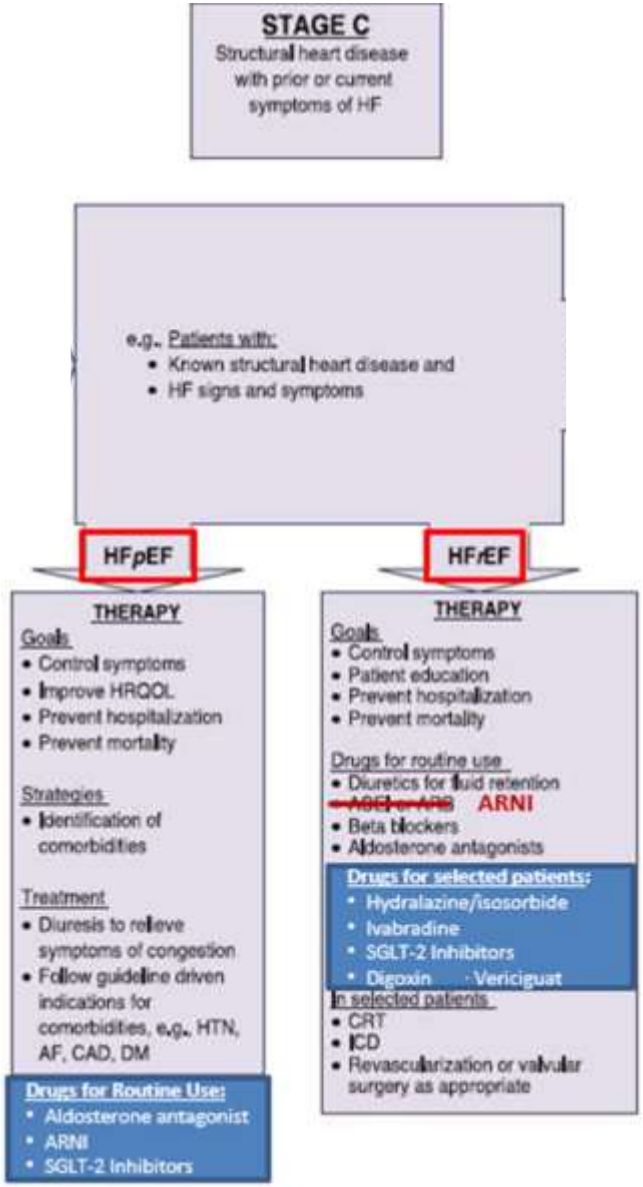
- Vericiguat
- Device therapy



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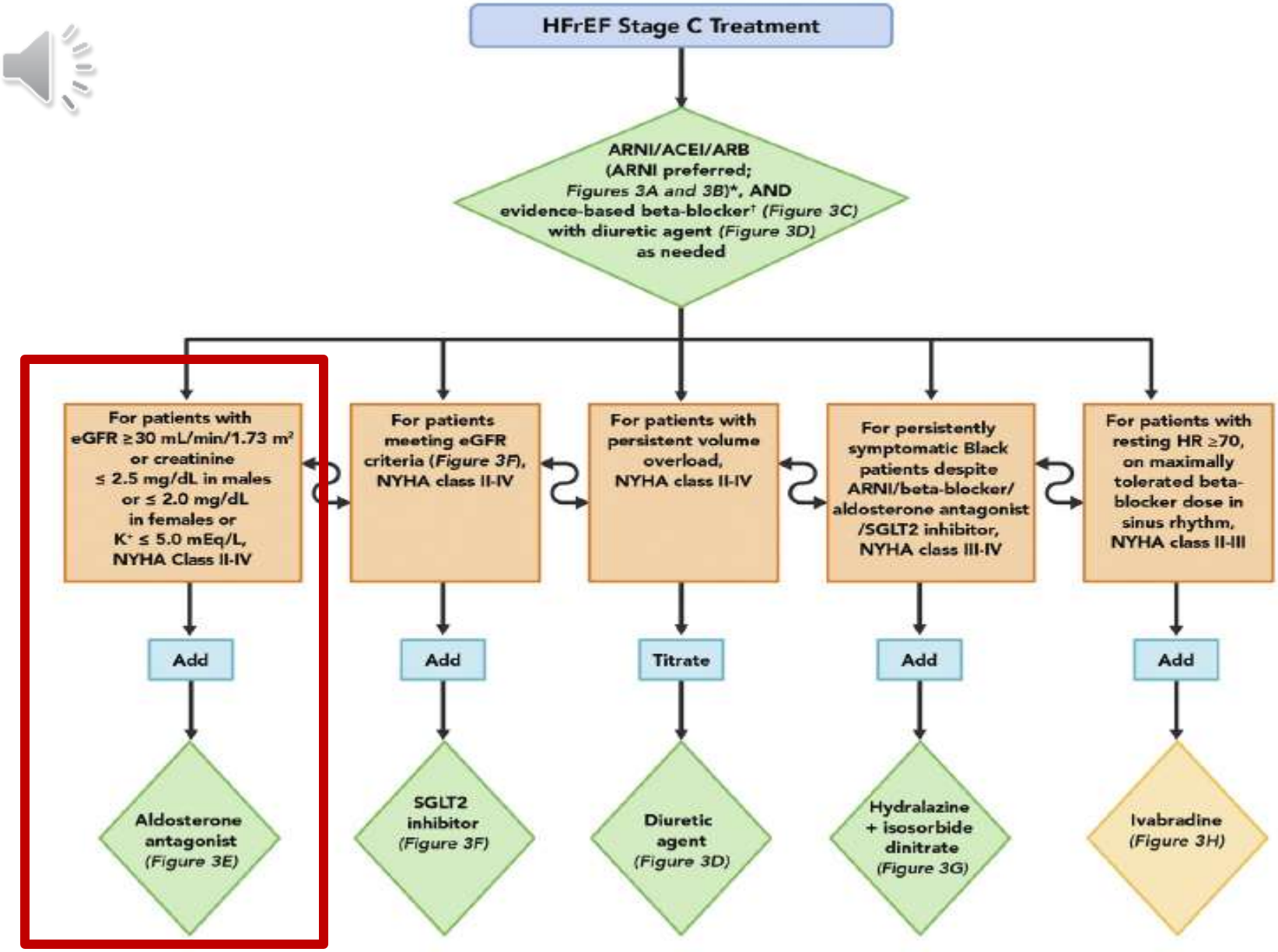

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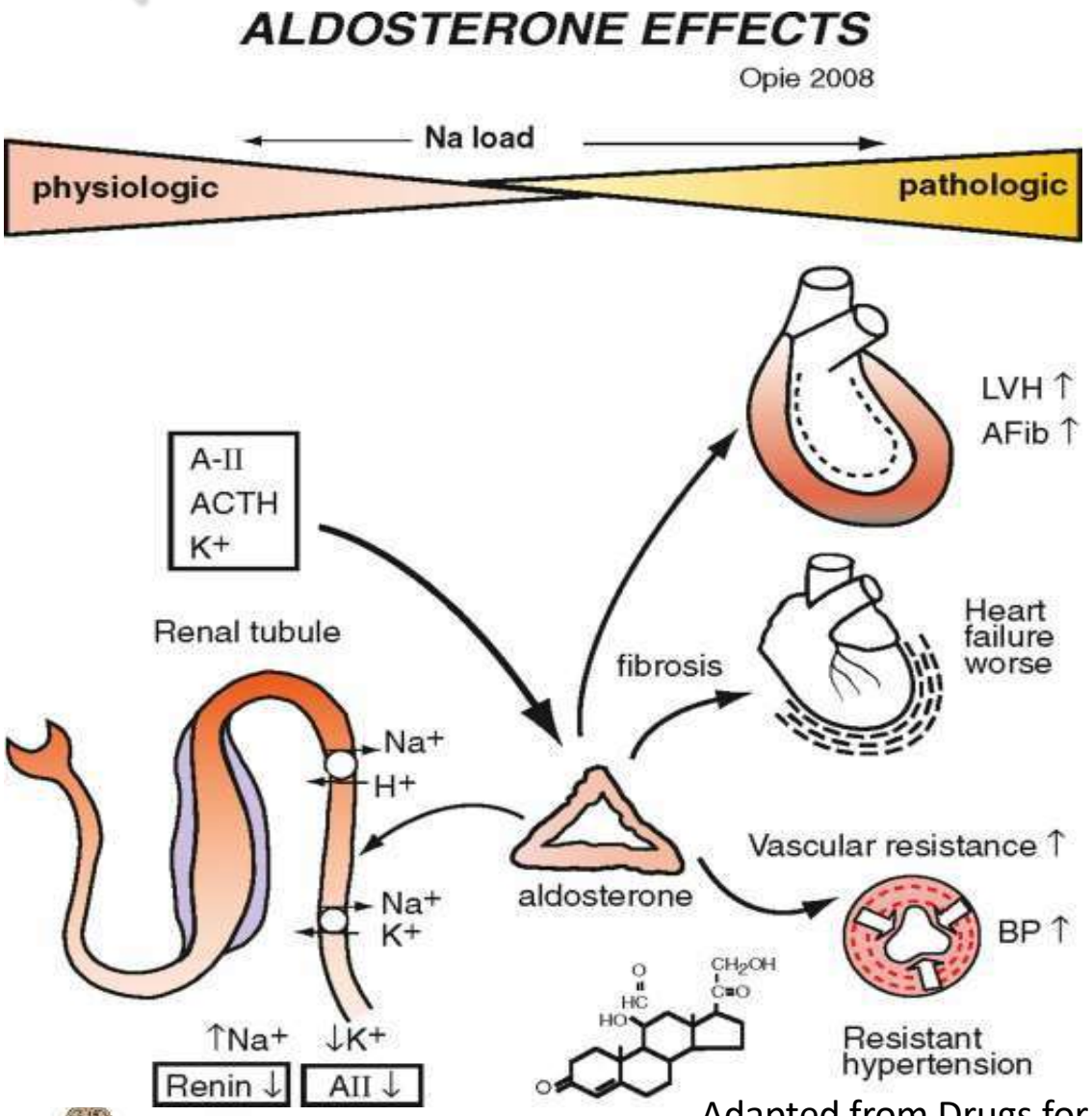
Aldosterone Antagonists



HF MOA:

1.

2.

3.

Adapted from Drugs for the Heart, 7th Edition. Figure 5-12

AA in HF

- Increased aldosterone concentrations contributes to congestion, atrial arrhythmias, myocardial remodeling, and sudden death
- Plasma aldosterone levels are elevated in HF despite blockade with ACEI or ARB therapy ("aldosterone escape")
- When added to GDMT, AA decreases hospitalizations and mortality and improves HF functional class
- **Criteria for use (Stage C HFrEF): EF ≤ 35% AND CrCl > 30 ml/min/1.73 m^2 (or SCr ≤ 2.5 mg/dL in men, ≤ 2 mg/dL in women) AND potassium level < 5 mmol/L**

2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment

AA Key Points

Side Effects:

- Gynecomastia, breast tenderness, hirsutism, menstrual changes
  - Eplerenone (Inspra) has higher affinity for mineralocorticoid receptors than for steroid receptors, producing fewer steroid-like side effects than spironolactone

- Hyperkalemia (may be life-threatening)
  - Stop potassium supplements with initiation of AA
  - Avoid high-potassium containing foods
  - Avoid triple therapy (ACEI + ARB + AA)
    - ACEI + ARB combo therapy is rare in HFrEF
  - Check within 2-3 days of initiation, 7 days after initiation, monthly for 3 months, and every 3 months afterwards

AA Dosing for HF*r*EF

	Initial Dose (if K+ </= 5 mEq/L)	Maintenance Dose
Spironolactone	**CrCl >/= 50 mL/min:** 12.5-25 mg QD	25mg QD-BID
	CrCl 30-49 mL/min: 12.5 mg QD or QOD	12.5-25mg QD
Eplerenone (Inspra)	**CrCl>/= 50 mL/min:** 25mg QD	50 mg QD
	CrCl 30-49 mL/min: 25 mg QOD	25 mg QD

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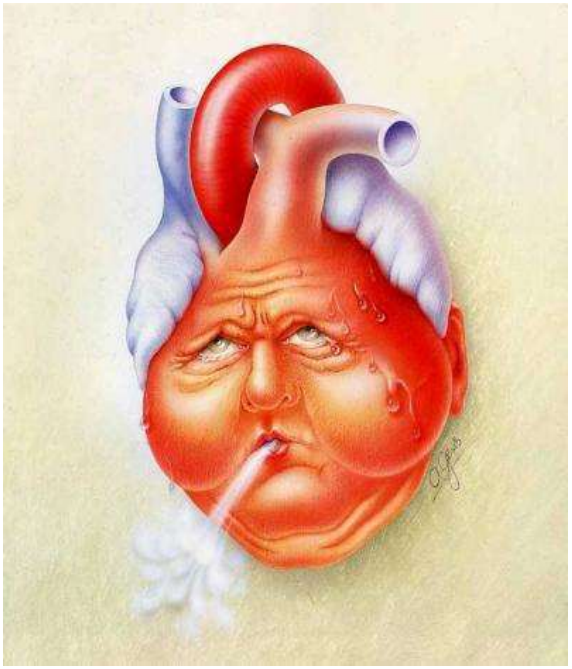
HF Part 6



- Medication therapies for stages in the development and progression of HF
  - Stage C: ARNI, hydralazine-isosorbide, and AA
- Patient case continued

Part 7: Medications for HF
Stage C: More meds and devices
Stage D
Medication therapies for HF*p*EF

HF Case: Part 2

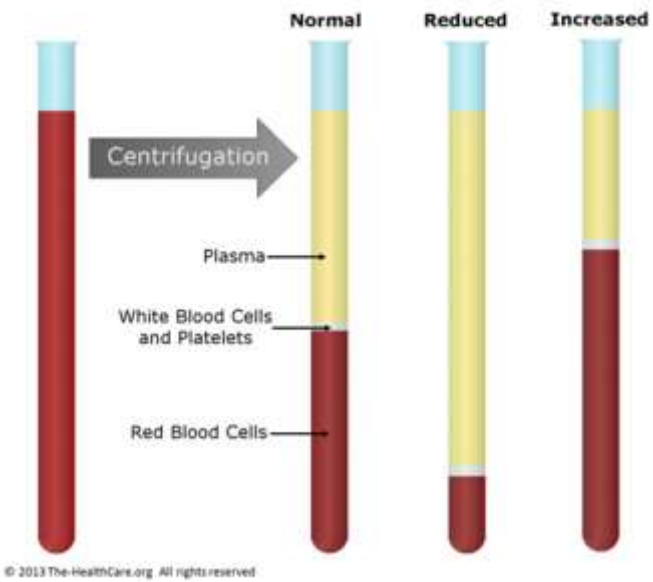
- SB is a 64 yo female who presents to clinic complaining of SOB with getting dressed and difficulty sleeping at night due to coughing.
- She notices her ankles are swollen and her socks leave a pronounced mark on her legs.
- She feels nauseous and gets full after eating only half of her meals.
- She can't exercise lately due to fatigue and weakness.

Question #5

- She is currently not receiving any guideline directed medications for HF. What medication(s) should you consider starting once she is at or near euvolemic?
  a. Carvedilol
  b. Lisinopril
  c. Metoprolol tartrate
  d. Valsartan
  e. Valsartan/sacubitril (?)

Question #6

- What labs would you like to order?
  - CBC: H/H
  - Chem 7: Na, K, BUN, SCr, Mg
  - LFTs
  - BNP (ACEI/ARB), NT-proBNP (ARNI)



- When would you like the patient to return to clinic for her lab checks?
  - 1-2 weeks after starting ARNI

HF Case: Part 3

- SB returns to clinic after 3 months for follow up.

- Today she is euvolemic and complains of SOB when trying to exert herself, such as when rushing to catch an elevator.

HF Case Continued

- Vital Signs: BP 118/68 mmHg, P 60 bpm
- Labs: K+ 4.3 mEq/L, SCr 1.4mg/dL
- Her medications include:
  - Valsartan/sacubitril 49/51 mg BID
  - furosemide 20mg daily
  - carvedilol 12.5mg twice daily
  - aspirin 81mg daily
  - atorvastatin 40mg daily
  - lansoprazole 30mg daily
  - NTG 0.4mg prn (has not needed)

Question #7

- What is the most appropriate choice for her treatment of HF?
  a. Add spironolactone 25mg daily
  b. Increase carvedilol to 25mg BID
  c. Increase furosemide to 20mg BID
  d. Increase valsartan/sacubitril to 97/103 mg BID
  e. Add hydralazine/isosorbide 37.5/25mg TID